#10 Amdt 4/29/01

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IN THE UNITED STATES PATENT & TRADEMARK OFFICE

IN RE APPLICATION OF:

AKIHIRO KISHISHITA ET AL : EXAMINER: ZUCKER

SERIAL NO. 09/708,006

FILED: NOVEMBER 8, 2000 : GROUP ART UNIT: 1623

FOR: NOVEL ASPARTAME DERIVATIVE: CRYSTAL AND PROCESS FOR PRODUCING THE SAME

DECLARATION UNDER 37 C.F.R. § 1.132

ASSISTANT COMMISSIONER FOR PATENTS
WASHINGTON, D.C. 20231

SIR:

Now comes KAZUTAKA NAGASHIMA who deposes and states:

1. That I am a graduate of Mie University and received my bachelor's degree in the year 1987 and master's degree in the year 1989.

2. That I have been employed by Ajinomoto Company Inc. for twelve years as a process engineer in the field of separation and purification.

3. That the following experiments were carried out by me or under my direct supervision and control.

4. Type A crystals of N-(3,3-dimethylbuty1)-APM are characterized by a X-ray diffraction peak of 6.0° (see Fig. 1 of the disclosure), whereas the C-type crystals of the present invention are characterized by a X-ray diffraction peak at 7.1° (see Fig. 2 of the disclosure). Each of these crystal types is also characterized by other X-ray diffraction peaks as shown in Figures 1 and 2 of the disclosure.

5. The following experimental data shows that the C type N-(3,3-dimethylbutyl)-APM ("Neotame") crystal of the present invention, which is characterized by an X-ray diffraction peak at 7.1°, is not obtained using the processes and recrystallization methods described by Nofre et al.,US Patent 5,480,668. Crystals prepared using the procedures described by Nofre et al, have the X-ray diffraction patterns of A-type crystals, which are characterized by a peak at 6.0°. Compare Fig. 1 of the disclosure with Figures 2-7 attached to this declaration. These figures are further described in the Experimental Examples below.

6. Experimental Example 1-- Recovery of N-(3,3-dimethylbutyl)-APM from methanol. Nofre et al., col. 7, lines 43-45 describe recovery of N-(3,3-dimethylbutyl)-APM from a methanol solution. For comparison to the procedure described by Nofre et al., N-(3,3-dimethylbutyl)-APM (5.0 g) having a water content of 4.1 % by weight was added to 100 ml of methanol. The mixture was stirred for 5 minutes at 40°C to prepare a homogeneous solution. This solution was then concentrated under reduced pressure at 30°C to remove methanol by distillation, and dried under reduced pressure at 40°C for 2 hours to produce dried powder (4.3 g) having a water content of 1.4 % by weight. The powder X-ray diffraction (X-ray diffraction pattern) of the dried powder was measured. As shown in the Figure 1 attached to this declaration, this powder was an amorphous product which did not show a clear diffractive X-ray pattern.

7. Experimental Example 2--Recovery of N-(3,3-dimethylbutyl)-APM from saline solution. Nofre et al., col. 7, lines 45-47 describe the recovery of N-(3,3-dimethylbutyl)-APM from a neutralized aqueous solution. For comparison to the procedure described by Nofre et al., 1 mol/l of NaCl (sodium chloride) aqueous solution (7.8 ml) was added at room temperature to the dried powder obtained in Experimental Example 1. Solid material was separated by filtration to obtain wet solid material (6.1 g) having a water content of 36 % by weight. The wet solid material (4.8 g) was then dried for 2 hrs under reduced pressure at 40°C to obtain dried powder (2.8 g) having a water content of 4.2 % by weight. The powder X-ray diffraction patterns of the thus obtained wet solid material and dried powder were

measured. Figures 2 and 3 attached to this declaration show that both the wet and dry powder were A-type crystals as determined by their X-ray diffraction patterns having a peak at 6.0° characteristic of A-type crystals.

8. Experimental Example 3: Recrystallization of N-(3,3-dimethylbutyl)-APM from acetonitrile. Nofre et al., col. 7, lines 47-51 describe recrystallization of N-(3,3-dimethylbutyl)-APM from acetonitrile. For comparison to the procedure described by Nofre et al., acetonitrile (2.3 ml) was added to 1.5 g of the dried powder obtained in Experimental Example 2. The mixture was stirred at 40°C for 5 minutes to prepare a homogeneous solution. This solution was subjected to a crystallization step overnight at 5°C. The solution was then filtered to obtain wet crystals (1.0 g) having a water content of 5.9 % by weight. Subsequently, the wet crystals (0.66 g) were dried under reduced pressure at 40°C for 2 hours to obtain dried crystals (0.62 g) having a water content of 4.3 % by weight. The powder X-ray diffraction pattern of the thus obtained wet and dry crystals was measured. Figures 4 and 5 attached to this declaration show that both the wet and dry crystals obtained by this method were A-type crystals as determined by their X-ray diffraction patterns having a peak at 6.0° characteristic of A-type crystals.

9. Experimental Example 4--Recovery of N-(3,3-dimethylbutyl)-APM from ethanol/water solution. Nofre et al., col. 7, lines 47-51 describe recrystallization of N-(3,3-dimethylbutyl)-APM from an ethanol/water (1/1) solution. For comparison to Nofre et al., an ethanol/water (1/1) solution (1.2 ml) was added to 1.2 g of the dried powder (1.2 g) obtained in Experimental Example 2, and the mixture was stirred at 40°C for 5 minutes to prepare a homogeneous solution. This solution was subjected to a crystallization step overnight at 5°C, and was then filtered to obtain wet crystals (0.84 g) having a water content of 18 % by weight. Subsequently, the wet crystals (0.51 g) were dried for 2 hrs under reduced pressure at 40°C to obtain dried crystals (0.44 g) having a water content of 4.3 % by weight. The powder X-ray diffraction pattern of the wet crystals and dried crystals was

measured. Figures 6 and 7 attached to this declaration show that both the wet and dry crystals obtained by this method were A-type crystals as determined by their X-ray diffraction patterns having a peak at 6.0° characteristic of A-type crystals.

10. The undersigned petitioner declares further that all statements made herein of his own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of this application or any patent issuing thereon.

11. Further deponent saith not.

Kazutaka Nozaki
Signature

September 7, 2001
Date

Fig. 1

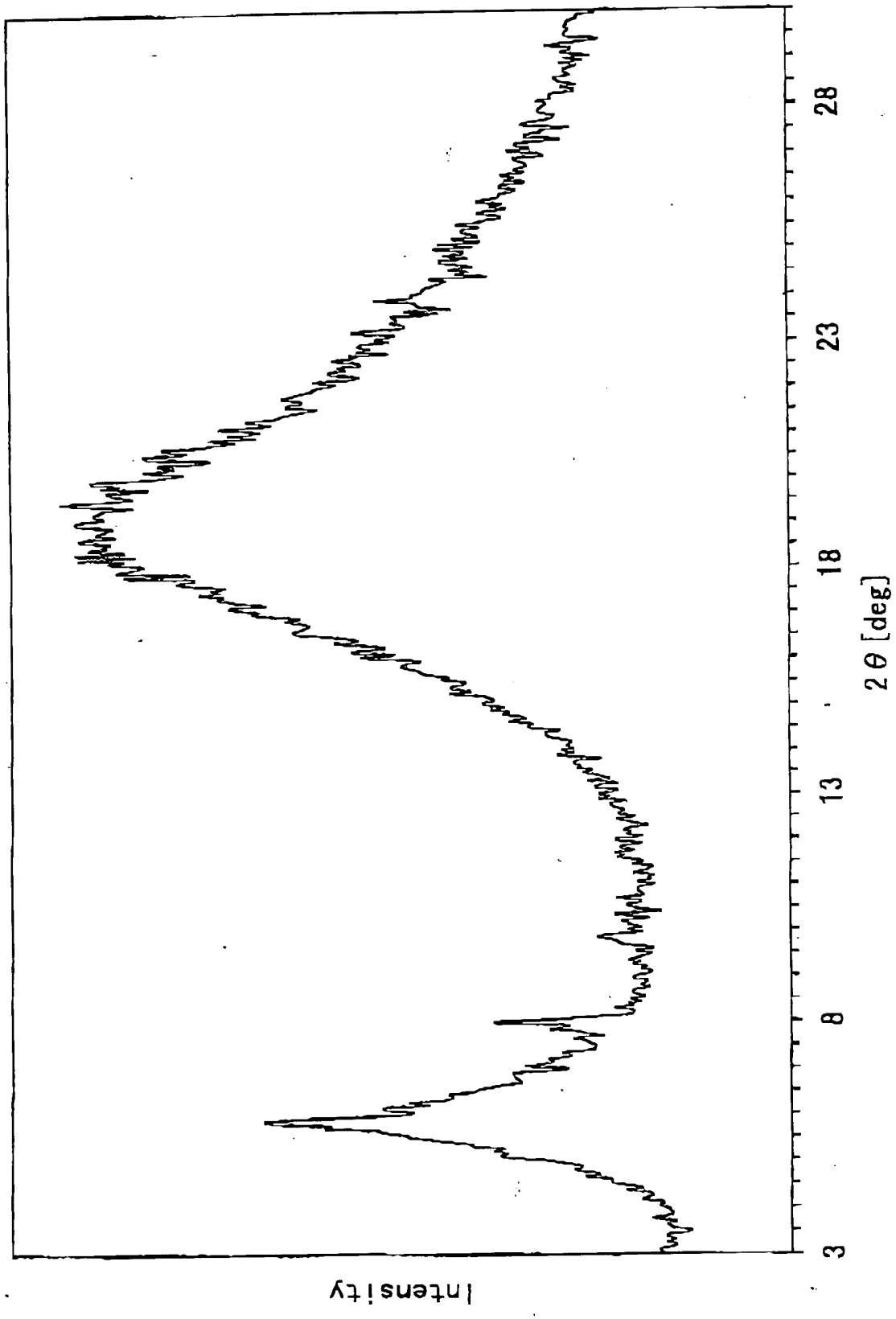

Fig. 2

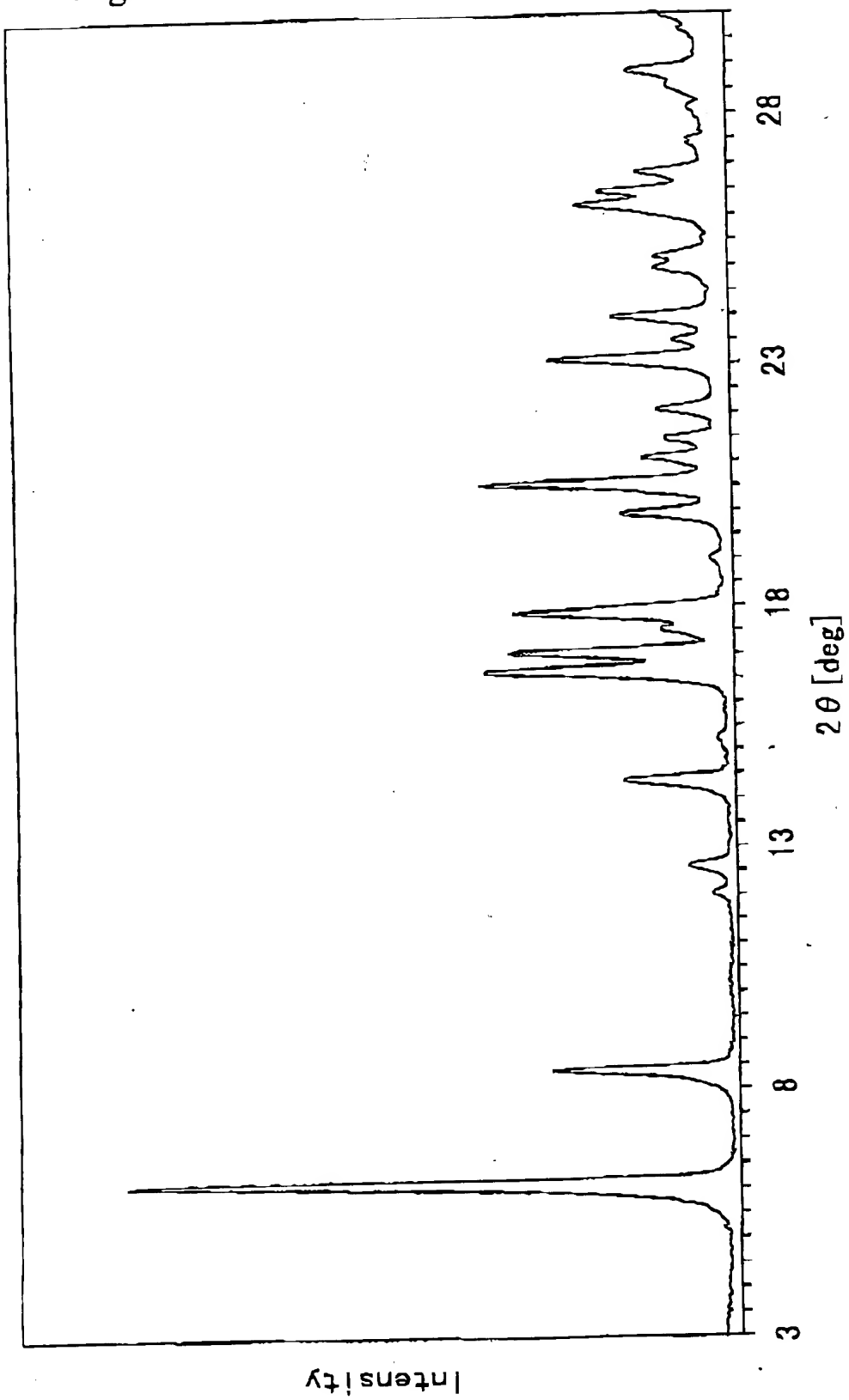

Fig.3

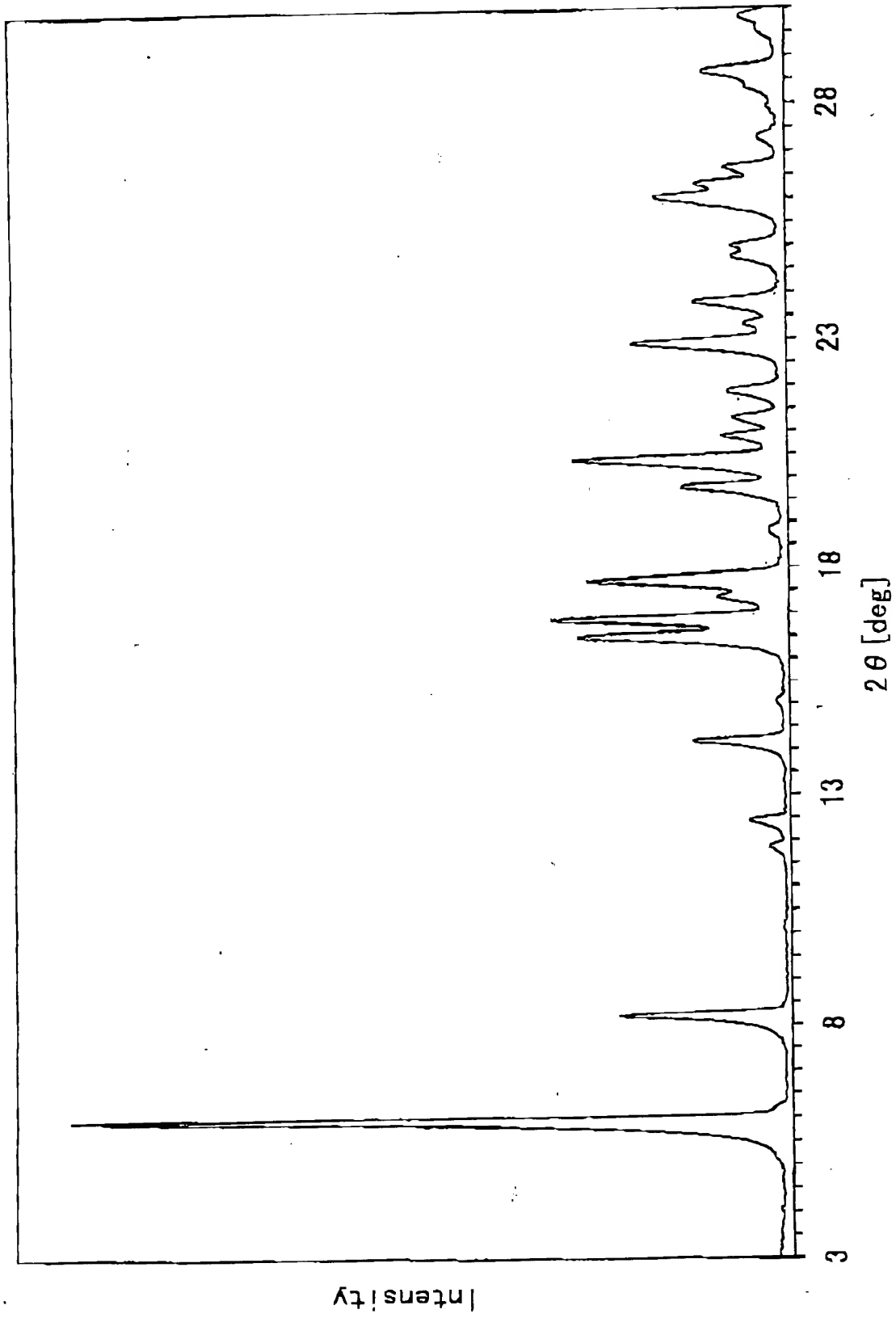

Fig. 4

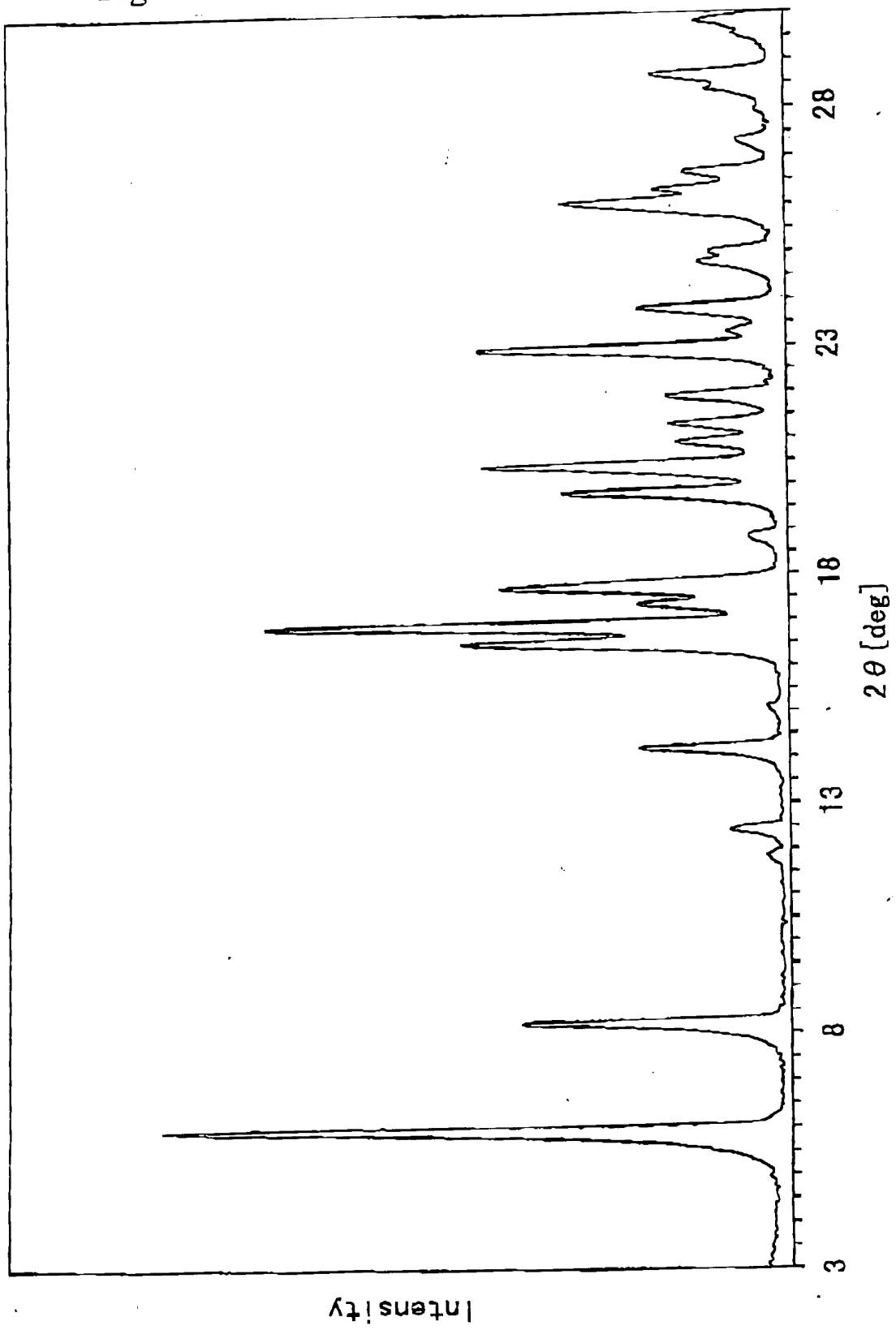

Fig. 5

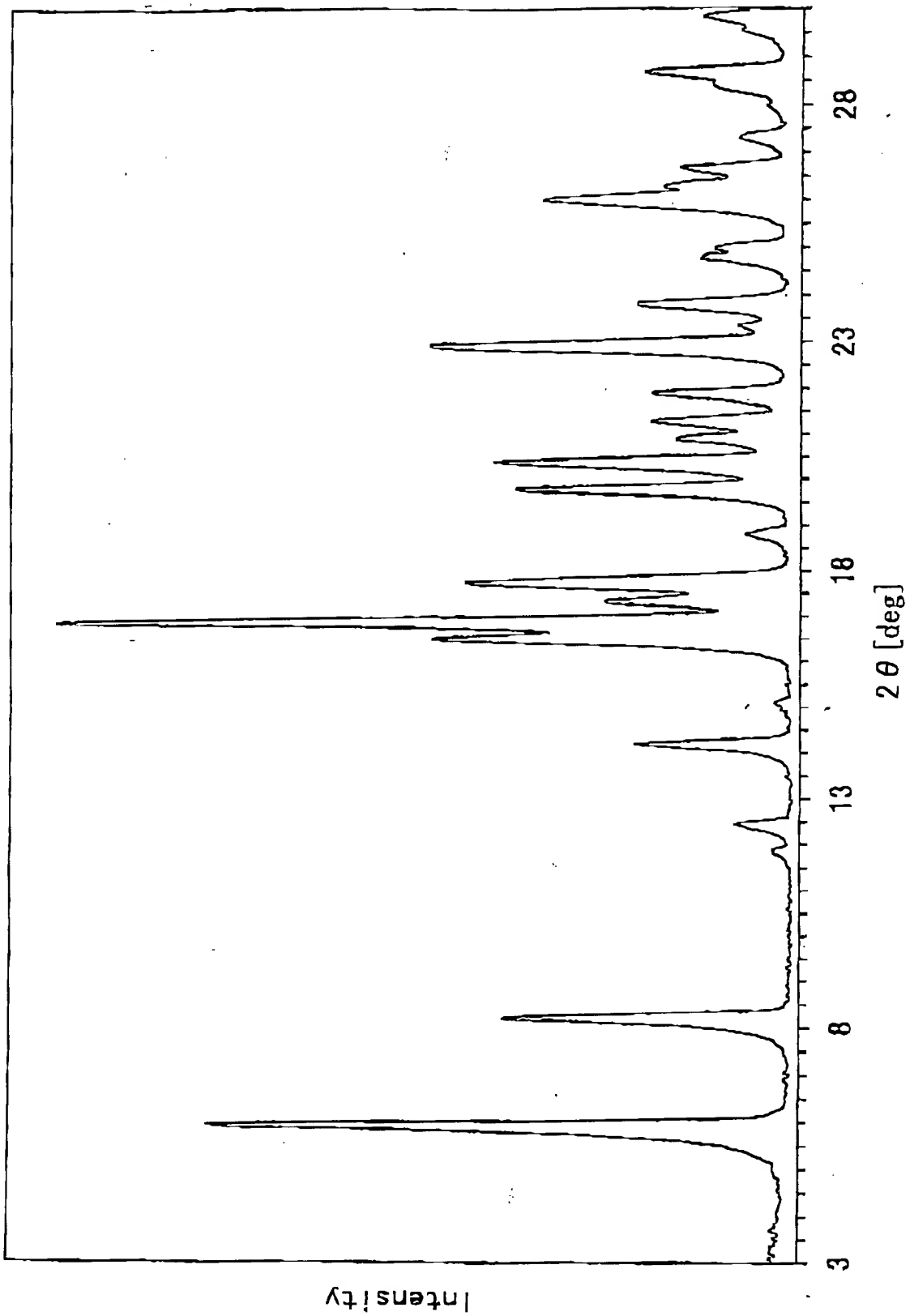

Fig. 6

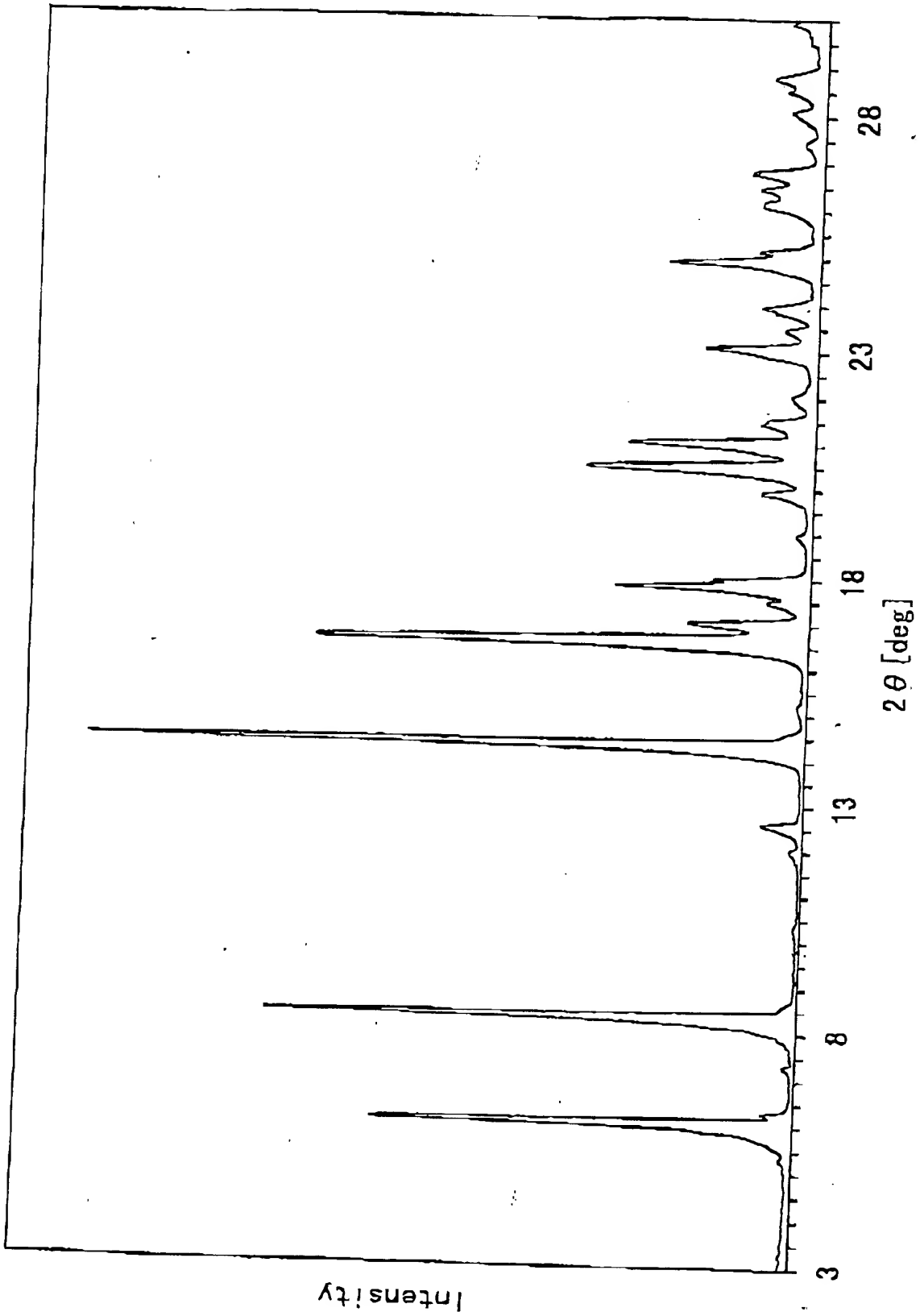

Fig. 7